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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/961,086	09/21/2001	Douglas D. Ross	028754-039	6592

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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/961,086	ROSS ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *March 31, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *5-7 and 13-15* is/are pending in the application.

4a) Of the above claim(s) *13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to you 37 CFR 1.114. Applicant's submission filed on December 9, 2004 is acknowledged and has been entered.

2. Claims 5, 13-15 have been amended. Claims 13-15 remain withdrawn from consideration as being drawn to non-elected inventions. Claims 5-7 are currently under prosecution. It is noted that Applicants request rejoinder of method claims 13-15 with pending claims 5-7 because according to MPEP 821.04, "if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined." MPEP 800-63. As currently amended, withdrawn process claims 13-15 depend from claims 5-7, and include all the limitations thereof. As claims 5-7 are now believed to be in allowable form, rejoinder of process claims 13-15 would appear to be in order. The request has been considered but has not been granted because claims 5-7 are not allowable for the reasons set forth below. Examiner notes, for Applicant's convenience, that process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Bouwer* and 35 USC 102(b),: 1184 O.G. 86 (March 26, 1996).

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. Claims 5-7 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of an antibody which "binds specifically" to SEQ ID NO:1 in claim 5 has no clear support in the specification and the claims as originally filed. A review of the remarks submitted on December 12, 2004 reveals that Applicant has mot submitted any citations from the specification or claims as originally filed that would support the newly added limitation. A review of the specification, as originally filed reveals two instances of the term "specifically" in the specification and claims as originally filed. In particular the term is found in paragraph 0039 of the published application:

> "More **specifically**, (emphasis added) the scope of the present invention is intended to include functional derivatives of BCRP which lack one, two, or more amino acid residues, or which contain altered amino acid residues, so long as such derivatives exhibit the capacity to influence cell resistance to chemotherapy."

And in paragraph 0071 of the published application:

> "An MCF-7/AdrVp cDNA library was constructed using the CapFinder.TM. PCR cDNA library construction kit (Clontech) according to the manufacturer's protocol. The CapFinder.TM. technique is designed **specifically** (emphasis added) to produce full-length double stranded cDNA."

Neither reference to the term "specifically" is drawn to antibody binding. Further, a review of the specification drawn to antibodies reveals only that, as set forth in the originally filed claims, that claim 5 recites "An antibody which binds to the protein of claim 1". The subject matter claimed in claims 5-7 broadens the scope of the invention as originally disclosed in the specification.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 5 and 7 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

The claims, as written, embrace naturally occurring antibodies to SEQ ID NO:1. Applicant suggests that SEQ ID NO:1 is a cancer antigen, associated with breast cancer, for multidrug resistance. The specification teaches that the claimed novel xenobiotic transporter is overexpressed in a variety of drug-resistant cancer cells (para 0006 of the published application). Although the specification does not teach that autoantibodies are generated against SEQ ID NO:1, Oches of Scripps Research Institute reveals the results of a study of autoantibodies in breast cancer (http://www.cbcrp.org/research/PageGrant.asp?grant_id=198) wherein it was disclosed in the final report in 1998 that "Autoantibodies in cancer patients appear to increase in amount, immediately preceding or coincident with the malignancy. It seems likely that these autoantibodies represent an immune response to abnormally ..... overexpressed proteins." The authors found that "A number of different autoantibody types were present, including antibodies against nucleoli, nuclear bodies, mitochondria, and the mitotic apparatus. Most of the other autoantibodies await further molecular characterization." Given the above, it would appear that it is more likely than not that the overexpressed antigen of the instant invention gives rise to autoantibodies. Thus, the claims as currently constituted appear to encompass the products as they occur in nature. However, since it would appear

that applicants do not intend to claim a naturally occurring product, amending the claims to recite isolated or purified antibody would obviate this rejection.

Claim Rejections - 35 USC § 103

7. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Purnelle et al (GenBank, Sequence Database Accession P25371), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available 1 May 1992 or Kirby et al (GenBank, Sequence Database Accession Q94960), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available February 1, 1997 and further in view of Harlow et al, of record.

It is noted Roitt et al (Immunology, 1993, Mosby, St. Louis, p 6.4-6.5) specifically teach that when the determinants of antigen A are shared by another antigen, B, then antibodies that bind to those determinants in A will also react with B. This phenomenon is termed cross-reactivity (see Fig 6.8 on page 6.4 and p. 6.5, para 1), thus antibody to an epitope that "binds specifically" to a particular antigen will also bind specifically to other proteins that share the same epitope. Further, Herbert et al (The Dictionary of Immunology, Academic Press, 3rd Edition, London, 1985, pges 58-59). specifically teach that an epitope is the region on an antigen molecule to which antibody specifically binds. Antibodies bind in a more or less exact three dimensional fit with an epitope (p. 58), thus the exact constitution of the amino acids forming the epitope is not critical as long as their three-dimensional fit produces an epitope to which the antibody will bind. Given that it is understood in the art that conservative substitutions are amino acid replacements that preserve the structure and functional properties of proteins, it would be expected that any protein that comprises five or more consecutive amino

acids that either share identity with or are conservative substitutions for amino acids found in another antigen would cross react with antibodies bind to the said five or more amino acid residues.

The claims are drawn to an antibody which binds specifically to SEQ ID NO:1 (claim 5), which is a monoclonal (claim 6), polyclonal antibody (claim 7).

Purnelle et al teach a polypeptide with 30.5% identity to SEQ ID NO:1 over 643 amino acid residues (see attached us-09-961-086-1.rsp, Result 3, Genbank P25371. It is noted that the polypeptide sequence of Purnelle et al shares multiple sets of five or more consecutive amino acids that either share identity with or are conservative substitutions for amino acids found in SEQ ID NO:1, a subset of which would be expected to comprise antibody epitopes shared with SEQ ID NO:1.

Kirby et al teach a polypeptide with 32.1% identity to SEQ ID NO:1 over 605 amino acid residues (see attached us-09-961-086-1.rspt, Result 15, Genbank Q94960). It is noted that the polypeptide sequence of Kirby et al shares multiple sets of five or more consecutive amino acids that either share identity with or are conservative substitutions for amino acids found in SEQ ID NO:1, a subset of which would be expected to comprise antibody epitopes shared with SEQ ID NO:1.

The references teach as set forth above but do not teach monoclonal, polyclonal antibody to SEQ ID NO:1.

Harlow et al teach that monoclonal antibodies are often more time-consuming and costly to prepare and they are not necessarily the best choice for certain immunochemical techniques. Although in theory, monoclonal antibodies can be used for all of the tasks that require or benefit from the use of polyclonal

antibodies, in practice, producing exactly the right set of monoclonal antibodies is often a difficult and laborious job (p. 142). The reference teaches specifically immunochemical techniques for which polyclonal antibodies are usually good including cell staining, immunoprecipitation and immunoblots (see Table 6.1, p. 142).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced monoclonal antibodies to both or either of the polypeptide of Kirby et al and Purnelle et al because the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of monoclonal antibodies against it is prima facie obvious. See Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1987), Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Bd. Pat. App. & Int. 1990). Given that no particular amino acid sequence to which the antibody binds is defined either in the specification or the claims as currently constituted, it would expected that at least a subset of the monoclonal antibodies produced against the polypeptide of Kirby et al and Purnelle et al protein would specifically bind SEQ ID NO:1 because these polypeptides share multiple sets of five or more consecutive amino acids that either share identity with or are conservative substitutions for amino acids found in SEQ ID NO:1 (a subset of which would be expected to comprise antibody epitopes shared with SEQ ID NO:1) and because it is known in the art that specific binding is drawn to common epitopes rather than to specific sequences.

Further, it would have been *prima facie* obvious and one would have been motivated to produce polyclonal antibodies to the polypeptides of either Purnelle et al or Kirby et al because Harlow et al specifically teach that monoclonal antibodies

are often more time-consuming and costly to prepare and they are not necessarily the best choice for certain immunochemical techniques. Although in theory, monoclonal antibodies can be used for all of the tasks that require or benefit from the use of polyclonal antibodies, in practice, producing exactly the right set of monoclonal antibodies is often a difficult and laborious job and polyclonal antibodies are useful for cell staining, immunoprecipitation and immunoblot techniques. Given the conventional nature of the production of polyclonal antibodies at the time the invention was made, one would have had a reasonable expectation of successfully producing antibodies to a breast cancer resistance protein.

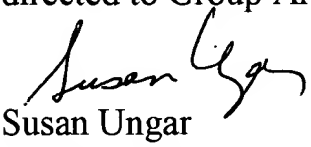
Finally, it is noted that the specification teaches at paragraph 0077 of the published application that "A "FASTA" comparison of the BCRP amino acid sequence revealed a high degree of homology to at least 50 ATP-binding cassette transport proteins. The highest match was PIR2:G02068, the human homologue of the Drosophila white (.omega.) gene, which has 638 amino acids, and is 29.3% identical to BCRP. The .omega. gene in Drosophila functions in the cellular transport of guanine and tryptophan, which are retinal pigment precursors (9)." Given that all of the references drawn to item 9 were published prior to 1990 it appears that multiple AP-binding cassette transport proteins, with sufficient homology with SEQ ID NO:1 to make it reasonable to expect that a subset of antibodies produced against those homologous polypeptides would also bind specifically to SEQ ID NO:1, were known in the art at the time the invention was made.

8. No claims allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.



Susan Ungar
Primary Patent Examiner
June 6, 2005